

Septic shock after medical abortions with mifepristone (Mifeprex, RU 486) and misoprostol

Reason for posting: Mifepristone is used with misoprostol to terminate early pregnancies and has been taken by more than 460 000 women. The US Food and Drug Administration (FDA) recently advised of 4 women in the United States who died of sepsis after taking the drugs for medical abortion. Two of the women had *Clostridium sordellii*-related sepsis (www.fda.gov/cder/drug/advisory/mifeprex.htm). A Canadian woman died in 2001 of *C. sordellii*-related septic shock after taking the drugs in a clinical trial.¹

The drugs: Mifepristone is a progesterone receptor antagonist and abortifacient, but was originally investigated for its antiglucocorticoid effects as a potential treatment for Cushing's syndrome. Widely used in Europe and the United States, it is not licensed for use in Canada. According to the FDA-approved protocol, 600 mg of mifepristone is taken orally within 49 days after the start of a woman's last menstrual period. Two days later 400 µg of the prostaglandin misoprostol is taken orally to soften the cervix and induce uterine contractions if the pregnancy has not already ended. Ten days later the woman is followed up clinically, often with ultrasonography, to confirm termination of her pregnancy. Complete medical abortion occurs in about 92% of women taking the regimen, but 5%–8% require a surgical procedure because of incomplete abortion, excessive bleeding or continuing pregnancy. Common adverse effects of the regimen include abdominal cramping and vaginal bleeding, headache, nausea and vomiting, and diarrhea. Rare but fatal cases of ruptured ectopic pregnancy have occurred. Mifepristone is metabolized in the liver by CYP3A4.

The 4 FDA-reported deaths occurred between 2003 and 2005

in California and involved women who had taken the misoprostol (800 µg) intravaginally. The infective agent was not identified in 2 of the cases. The patients with *C. sordellii* infection apparently had similar presentations (Box 1).

C. sordellii is a gram-positive anaerobe found ubiquitously in soil and as part of the human intestinal flora. Ten percent of women's vaginas are colonized. Infections are rare but have been reported in patients of all ages with both intact and compromised immune systems. Death is common, and the infections often occur after transcuteaneous, perineal or gastrointestinal procedures.² The organism produces an endotoxin and can produce 2 potent exotoxins. *C. sordellii* sepsis in mifepristone users may occur through effects on cortisol or cytokine responses.³

What to do: Women should be warned of this rare but potentially fatal adverse effect. They should seek immediate attention if they have fever, severe abdominal pain, very heavy bleeding, syncope or general malaise. However, clinicians must be aware that all of the deaths from *C. sordellii* sepsis reported here involved symptoms listed in Box 1. Prophylactic antibiotic therapy is not recommended for all women undergoing medical

Box 1: Characteristics of *Clostridium sordellii* septic shock after medical abortion with mifepristone and misoprostol

- Little or no fever
- Variable nausea, vomiting, weakness and abdominal pain (often little)
- Rapid deterioration (within hours or days)
- Tachycardia and refractory hypotension
- Multiple effusions
- Elevated hematocrit
- Elevated leukocyte count, neutrophilia

abortion; however, for those with suspected sepsis, complete blood counts and necessary cultures should be obtained and aggressive, empirical treatment with antibiotics started that includes coverage against *C. sordellii*.

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